REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated October 23, 2002 and the Interview conducted on January 14, 2003.

Claims 1-4 are under consideration in this application. Claims 1-4 are being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Formality Rejection

The recitation of "detecting spots" in the claims has been rejected under 35 U.S.C. § 112, second paragraph, for failure to distinctly claim the invention. As indicated, the recitation has been amended as required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claims 1-17 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 98/22620 to Stanley (hereinafter "Stanley") in view the article by Burgart et. el. (hereinafter "Burgart"). This rejection has been carefully considered, but is most respectfully traversed.

The method of detecting PCR-amplified base sequences 42 of the invention, as now recited in claim 1, comprises: conducting PCR amplification by mixing a plurality of pairs of primers 31-33 with a sample, said primers being suitable for amplifying different base sequences, such as DNA (1), DNA(2), of a same length or different lengths by PCR; conducting a hybridization reaction by using a substrate 30 on which said primers used for the PCR are fixedly

spotted on spots thereon and a solution containing said base sequences that are PCR-amplified in the preceding step, said hybridization reaction being performed between the primers fixedly spotted on the substrate and said PCR-amplified base sequences; and detecting at least one of the spots on said substrate in which the hybridization reaction occurs. The key of the invention is to fix/implant different types of primers 31, 32, 33 (which may be of the same length) on different spots of a glass slide/ substrate 30 (page 9, lines 15-18) to hybridize with different types of DNAs so as to measure the fluorescence emitted from each spot corresponding to one type of PCR-amplified DNAs 42 derived from a respective type of primer (page 10, lines 25-28) and thereby determine the amount of different types of PCR-amplified DNAs .

Applicants respectfully contend that neither Stanley nor Burgart, nor their combination as relied upon by the Examiner, teaches or suggests "fixing different types of primers which may be of the same length on different spots on a substrate to detect the respective amount of different types of PCR-amplified DNAs".

In contrast, Stanley only amplifies one type of nucleic acid rather than different types of nucleic acids per PCR reaction tube. As acknowledged by the Examiner on page 3, line 18 of the outstanding Office Action, Stanley did not teach amplifying different types of nucleic acids per one PCR reaction tube, i.e., multiple PCR.

As to Burgart, although it teaches multiple PCR, its separation scheme is totally different from the invention. Burgart requires running ***a plurality of "no-target" reactions*** (i.e., negative controls having reaction mixtures containing all components except one target DNA) ***in addition to said one PCR reaction*** (page 320, col. 2, lines 1-6; page 321, col. 2, last paragraph). Thereafter, the detected results have to be *calculated* to find out the respective amount of different types of PCR-amplified DNAs.

On the other hand, the simple physical arrangement of different types of primers on different spots on the substrate accordingly to the invention allows the respective amount of different types of PCR-amplified DNAs to be *detected directly* without additional reactions or calculation. It is well established that a rejection based on cited references having contradictory principles or principles that teach away from the invention, such as **one** PCR reaction vs. **a plurality of** control reactions, or the incompatible separation schemes, is improper.

Contrary to the Examiner's allegation that one skilled in the art would be motivated to combine Stanley's detecting method with the multiple PCR in Burgart such

that the alleged combination would analyze multiple target sequences simultaneously on a solid support, Applicants respectfully contend that one skilled in the art can't derive such a conclusion as alleged based upon the cited paragraphs or any portions of Stanley or Burgart. Both Stanley and Burgart are solution-based. Neither Stanley nor Burgart mentions a solid support for the primers or fixing different types of primers on different spots on the solid support.

The Examiner's reliance upon the "common knowledge and common sense" of one skilled in the art for any motivation for combining the teachings in Stanley and Burgart or the alleged teaching of "a solid support" did not fulfill the agency's obligation to cite references to support its conclusions. Instead, the Examiner must provide the specific teaching of the combination on the record to allow accountability.

> *To establish a prima facie case of obviousness, the Board must, inter alia, show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." Kotzab, 217 F.3d at 1370, 55 USPQ2d at 1317. .... Recently, in In re Lee, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002), we held that the Board's reliance on "common knowledge and common sense" did not fulfill the agency's obligation to cite references to support its conclusions. Id. at 1344, 61 USPQ2d at 1434. Instead, the Board must document its reasoning on the record to allow accountability. Id. at 1345, 61 USPQ2d at 1435.*
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> See In re Thrift, 298 F.3d 1357.

Such an obligation to provide specific teaching(s) also applies to other existing or future obviousness rejections.

Even if, arguendo, a person of ordinary skill were motivated to combine the teachings in Stanley and Burgart as specified by the Examiner, such combined teachings would still fall short in fully meeting the Applicants' claimed invention as set forth in claim 1 since, as discussed, there are no teachings of "fixing different types of primers which may be of the same

length on different spots on a substrate to detect the respective amount of different types of PCR-amplified DNAs" in Stanley or Burgart.

Applicants contend that neither Stanley, Burgart, nor their combination teaches or discloses each and every feature of the present invention as disclosed in independent claim 1. As such, the present invention as now claimed is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

Respectfully submitted,

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Marked-up Version of Amended Claims

1. A method of detecting PCR-amplified base sequences, comprising the steps of:

conducting PCR amplification by mixing a plurality of pairs of primers with a sample, said primers being suitable for amplifying different base sequences of a same length or different lengths by PCR [individually];

conducting a hybridization reaction by using a substrate on which said primers used for the PCR are fixedly spotted on spots thereon and a solution containing said base sequences that are PCR-amplified in the preceding step, said hybridization reaction being performed between the primers fixedly spotted on the substrate and said PCR-amplified base sequences; and

detecting at least one of the spots on said substrate in which the hybridization reaction occurs.

2. The method of detecting PCR-amplified base sequences according to claim 1, wherein said step of detecting the spots on said substrate in which the hybridization reaction occurs includes the steps of:

processing a fluorescent material to enter in double-stranded DNA; and

detecting fluorescence generated by exciting said fluorescent material contained in [any] said at least one of the spots on the substrate.

3. The method of detecting PCR-amplified base sequences according to claim 1, wherein each of said primers has a base length number in a range from 10 to 30.

4. The method of detecting PCR-amplified base sequences according to claim 2, wherein each of said primers has a base length number in a range from 10 to 30.